particularly timely to discuss topical retinoic acid (tretinoin; Retin-A) in view of the recent, carefully managed spate of publicity surrounding this agent.

Is there solid evidence for its usefulness? Can physicians delineate specific indications for its use? Retinoic acid, the progenitor of several generations of synthetic retinoids,[1] exerts powerful effects on epidermal differentiation. By normalizing keratinocyte maturation, this agent can reverse and prevent preneoplastic changes, but only a few established skin cancers respond to either systemic or topical retinoids.[2]

Although the driving force for the development of the synthetic retinoids is the excessive toxicity of vitamin A and its derivatives, ironically, it may be the low-grade irritancy of retinoic acid that promotes its percutaneous delivery to the dermis, allowing this agent to exert its effects on mesenchymal elements in that layer. By stimulating fibroplasia, leading to de novo collagen and proteoglycan synthesis, retinoic acid displaces downward actinically damaged, elastotic collagen.[3] In addition to its effects on keratinocytes and fibroblasts, topical retinoic acid apparently can stimulate endothelial cell proliferation and pigment dispersal,[4] effects that also can improve the appearance of photodamaged skin. Retinoic acid has been appreciated longest for its impact on pilosebaceous structures: in addition to diminishing sebum output, retinoic acid may reduce the number of open and closed comedones. The former, in particular, are an additional stigmatum of photodamaged skin. Finally, in altering epidermal differentiation and accelerating shedding, topical retinoic acid can reduce much of the excess scale that can be a concomitant of aging skin. In fact, retinoids remain the most effective form of therapy for the ichthyoses,[5] a broad group of inherited and acquired disorders characterized by excess scale.[6]

Is topical retinoic acid a panacea for photoaging? Certainly not. The impact on extensively damaged, deeply furrowed skin is minimal. But the ability of this agent to reverse and prevent epidermal neoplasias—albeit not as effectively as 5-fluorouracil; stimulate the renewal of various cellular elements in the dermis; promote normal pigmentation; and reduce both excessive scale and follicular cornified material makes this agent, and perhaps generations of topical retinoids still to come, reasonable therapy for extensively photodamaged skin. Finally, there are obvious advantages to medical versus surgical therapy for extensively sun-damaged skin, although the use of topical retinoids does not preclude, and even may complement, such surgical interventions as dermabrasion, chemical peels, and collagen implantation.

Topical retinoids also hold promise as primary and adjunctive therapy for a variety of other cutaneous processes, including enhancing the healing of leg ulcers in patients receiving systemic steroids or nonsteroidal anti-inflammatory agents, reversing dysplastic changes in dysplastic nevi, treating a variety of mucosal ulcerative and scarring conditions, and stimulating hair growth. Much of this work is still preliminary and beyond the scope of this article but available to readers in two recently published symposia.[7,8]

Finally, the use of topical retinoids mandates certain precautions. Retinoids are not only antineoplastic but also potentially tumor *promoters* in certain photocarcinogenesis assays.[9] This, plus phototoxicity due to possible retinoid-ultraviolet A interactions or a diminished generation of protein products of epidermal differentiation, can produce photosensitivity. Hence, the use of broad-spectrum sunscreens (a sun protective factor of 15 or higher) is indicated, which use will also help prevent a further progression of the deleterious effects of sunlight. Topical retinoic acid is also an irritant and therefore particularly difficult to administer to patients with "sensitive" skin—that is, those with atopy. Yet, with patience and careful follow-up, the poorly understood phenomenon of "hardening" occurs, allowing almost anyone to use this agent. Finally, the consequences of long-term usage in the elderly are not known, although some adolescents and young adults have used topical retinoic acid for decades without problems.

In the final analysis, it is the treating physician who must decide whether retinoids are indicated medically, cosmetically, or both—that is, when is one prescribing legitimately versus pandering to the wishes of patients simply shopping for the latest cosmetic angle. In the latter case, the risks may outweigh the potential benefits.

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REFERENCES

1. Elias PM, Williams ML: Retinoids, cancer, and the skin. Arch Dermatol 1981; 117:160-180

2. Peck GL, DiGiovanna JJ, Sarnoff DS, et al: Treatment and prevention of basal cell carcinoma with oral isotretinoin. J Am Acad Dermatol 1988; 19 (pt 2):176-189

3. Kligman LH, Duo CH, Kligman AM: Topical retinoic acid enhances the repair of ultraviolet damaged dermal connective tissue. Connect Tissue Res 1984; 12:139-150

4. Weiss JS, Ellis CN, Headington CN, et al: Topical tretinoin improves photoaged skin: A double-blind vehicle-controlled study. JAMA 1988; 259:527-532

5. Peck GL, Yoder FW: Treatment of lamellar ichthyosis and other keratinizing dermatoses with an oral synthetic retinoid. Lancet 1976; 2:1172-1174

6. Williams ML, Elias PM: Genetically transmitted generalized disorders of cornification (the ichthyoses), *In* Alper JC (Ed): Dermatology Clinics of North America. Philadelphia, WB Saunders, 1987, pp 155-178

7. Topical retinoids, an update: Proceedings of symposium of the American Academy of Dermatology, New York, April 19-20, 1986. J Am Acad Dermatol 1986; 15 (pt 2)

8. Shalita A (Ed): Retinoids: Proceedings of a symposium, American Academy of Dermatology, San Antonio, Texas, December 8, 1987. J Am Acad Dermatol 1988; 19 (pt 2)

9. Forbes PD, Urbach F, Davis RE: Enhancement of experimental photocarcinogenesis by topical retinoic acid. Cancer Lett 1979; 7:85-90

Persistent Vaginitis

IN EVALUATING AND TREATING VAGINITIS and vaginal discharge, clinicians frequently face situations that are not straightforward.[1] Treatment choices often seem arbitrary, and failures occur. Confusion arises because of considerable variation in symptoms, coexistent infections, poor patient or partner compliance, and cultures that may not be specific.

Yeast Vaginitis

The organisms causing yeast vaginitis—*Candida albicans, Candida* species, and *Torulopsis glabrata*—can be identified in 10% to 30% of routine vaginal cultures because of high asymptomatic carrier rates.[2-4] Symptoms vary from minimal discomfort to intense itching or burning with associated vulvar erythema and abrasions. The vaginal discharge is scant to moderate, appears white and curdlike but may be thin and pasty, tends to adhere to vaginal walls, has no odor or smells musty, and has a pH of 4.0 to 5.0. A saline slide preparation shows a slight to a pronounced increase of leukocytes per high-power field. Adding potassium hydroxide shows mycelial forms. The highest yield will come from scrapings of vaginal sidewalls or the introitus.

The standard treatment of yeast vaginitis consists of applying miconazole or clotrimazole, 100 mg, to the vagina in

TABLE 1.—*Recommended Treatment for Persistent Vaginitis*

Type of Vaginitis	Treatment Regimen: Initial Infection	Treatment Regimen: Recurrent Infections	Recurrent or Refractory Infections
Yeast infection	Miconazole or clotrimazole, 100 mg at bedtime × 7 vaginally, *or* 200 mg × 3	Prolong therapy over 2-3 menstrual cycles; apply gentian violet; apply acidifying agents (vinegar douches, Aci-Jel)	Treat partner topically; check for condylomata; give maintenance dose of ketoconazole; review risk factors (diabetes, oral contraceptive use, antibiotic therapy, immunosuppressive therapy)
Trichomonas vaginalis	2 grams metronidazole orally, treat partner	500 mg metronidazole orally bid × 7 d; review sexual contacts; recommend condom use	1 gram metronidazole orally × 7 d; 100 mg clotrimazole vaginally × 7 d; betadine douches
Bacterial vaginosis	500 mg metronidazole orally bid × 7 days; may be useful to treat partner	Metronidazole, same dosage as for initial infections; treat partner; recommend condom use	Check for coexistent infections; evaluate upper tract; apply acidifying agents
Atrophic vaginitis	2-4 grams estrogen cream every night for 1-3 weeks, ½ to 1 applicatorful; taper to once or twice a week	Estrogen cream, as for initial episode	Consider estrogen replacement therapy

bid=twice a day

cream or suppository form for seven nights or 200 mg for three nights (Table 1). The cream may also be applied directly to the labia and groin. Persistent symptoms occasionally require a second treatment course.

Those at increased risk for recurrent or refractory infection include women with diabetes mellitus; obese or pregnant women; women with an impaired immune response; and those receiving antibiotic therapy, oral contraceptives, or immunosuppressive agents.

In patients with refractory infections, the presence of the fungal agent should be documented by vaginal culture or potassium hydroxide slide. Sometimes a neurodermatitis, lichen simplex chronicus, develops as a sequela to severe yeast infections, and topical corticosteroids are needed to relieve the pruritus.[5] Coexistent infections may occur. Condylomata can cause persistent itching or dyspareunia and may be overlooked during an active yeast infection. The vulvar mucosa often displays only subtle findings with a cobblestoned or fine papillary pattern. A simple punch biopsy of the vulvar mucosa will confirm the diagnosis.

For patients with recurrent yeast infections, the following recommendations may be helpful:

- Extend the course of therapy through two to three menstrual cycles. Either try administering miconazole, 100 mg nightly, from the beginning of one period through the end of the next period, or have the patient apply 100 mg of miconazole to the vagina for ten nights during each of three menstrual periods in a row.
- Treat the patient's sexual partner topically with miconazole cream applied to the penis (especially prepuce) and groin twice a day for ten days.
- Treat the patient prophylactically whenever antibiotics are administered.
- Gentian violet applied directly to the cervix, vagina, labia, and perianal mucosa is surprisingly successful. For persistent infections, repeat the application once or twice at weekly intervals or just before the menses.
- Finally, Sobel has shown excellent results using oral ketoconazole, 200 mg daily for six months, as long-term suppressive therapy.[6] When using this drug, surveillance for potential hepatic toxicity is necessary.

Patients should also be instructed in proper genital and toilet hygiene. Keeping the area cool and dry is important, and all-cotton underwear, not merely cotton-crotch varieties, aids in absorbing natural moisture. Some women find remedies designed to boost vaginal acidity can reduce the frequency of yeast infections. These would include Aci-Jel (an acidifying vaginal gel) or vinegar douches (two to three tablespoons to a quart of warm water) once or twice a week.

Bacterial Vaginosis

Bacterial vaginosis (formerly nonspecific vaginitis) is a condition of anaerobic bacterial overgrowth associated with *Gardnerella vaginalis, Bacteroides* species, and the more recently identified *Mobiluncus* species.[7-9] Although associated with sexual activity, the etiologic agent has not been pinpointed. *Gardnerella* organisms can be identified in as many as 20% of specimens from asymptomatic women and are found in screening cultures.[10,11] Also, coexistent infections are common.

Patients with bacterial vaginosis often lack inflammatory response, and their predominant symptoms are discharge or odor. The discharge appears homogeneous, thin or pasty, and can be white, gray, or yellow. The pH is usually 5.0 or higher. The anaerobic bacteria produce organic acids that cause the foul odor. When a drop of potassium hydroxide is added to a laboratory specimen—the amine or sniff test—these acids are converted to volatile amines and a fishy odor can be detected. This odor is transient and can be missed, but patients may notice it when their discharge comes in contact with soap or semen. A saline slide preparation will show normal to moderately increased leukocyte counts per high-power field and the presence of "clue" cells, epithelial cells studded with bacteria having a granular appearance.

A seven-day course of metronidazole, 500 mg twice a day, is more effective than giving ampicillin or sulfa creams. Routinely treating the partner is a controversial though acceptable practice but is a logical next step if infection recurs.

Trichomoniasis

Trichomonas vaginalis is a sexually transmitted protozoan causing vaginitis in women. Men harbor the organism in the paraurethral glands and prostate but are usually asymptomatic. A symptomatic woman will present with a malodorous discharge that can be scant to profuse, yellow or green, watery, and sometimes frothy. The pH is greater than 4.5. The classic "strawberry cervix," mucosal microabscesses studding the cervix, is rarely seen. Adding potassium hydroxide to a specimen often produces a positive sniff test, and the saline slide shows a moderate to substantially in-

creased leukocyte count. The diagnosis is confirmed by identifying the motile forms on a fresh saline slide. The protozoans are readily recognized by their random motion and beating flagella.

Treatment consists of 2 grams of metronidazole taken orally in a single dose for the patient and partner. Treatment fails most commonly when there is reinfection. Reviewing condom usage and the patient's sexual contacts and retreating with metronidazole usually resolve the infection. True antibiotic resistance is rare, but in cases of partial resistance, treating a patient with metronidazole, 500 mg twice a day for seven days, is successful.

Noninfectious Vaginitis

Noninfectious causes of vulvovaginitis include reactions to a variety of chemicals: medicated douches, iatrogenic agents, spermicides and sponges, feminine deodorants, and harsh soaps. Foreign bodies are a notorious cause in children, but in menstruating women a forgotten tampon is not uncommon. Discontinuing the irritating chemical or removing the foreign body results in a clearing of symptoms.

Atrophic vaginitis affects postmenopausal women and is caused by thinning and weakening of the vulvar and vaginal tissues, a rise in pH accompanying a loss of the glycogen content, and a subsequent bacterial overgrowth. Treatment consists of applying estrogen cream, 2 to 4 grams daily—equivalent to a half to a full applicatorful—for one to three weeks. As soon as symptoms subside, treatment should be tapered to once or twice a week at minimal dosages because significant systemic absorption may occur and lead to endometrial stimulation. If local, vaginal treatment is inadequate, systemic estrogen replacement therapy may need to be considered.

Upper Genital Tract

When vaginal discharge persists and vaginitis has been excluded, an upper tract source should be considered. Uterine problems include endometritis, irritation caused by an intrauterine device, polyps, and malignancy. In cases of suspected cervicitis, cultures for *Chlamydia,* gonorrhea, and herpes simplex virus should be done. The Pap test, colposcopy, and cervical biopsy are invaluable techniques for identifying cervical condylomata, cervical dysplasia, and cervicitis.

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REFERENCES

1. Hill LV, Embil JA: Vaginitis: Current microbiologic and clinical concepts. Can Med Assoc J 1986; 134(4):321-331

2. Jones GR, Warnock DW: Diagnosis of candida vulvovaginitis. J Clin Pathol 1978; 31:98-99

3. Leegaard M: The incidence of *Candida albicans* in the vagina of 'healthy young women.' Acta Obstet Gynecol Scand 1984; 63:85-89

4. Odds FC: Genital candidosis. Clin Exp Dermatol 1982; 7:345-354

5. Solomon LM: Chronic anal and vulvar pruritus, *In* Moschella SL, Hurley HJ (Eds): Dermatology. Philadelphia, WB Saunders, 1985, pp 384-388

6. Sobel JD: Recurrent vulvovaginal candidiasis: A prospective study of the efficacy of maintenance ketoconazole. N Engl J Med 1986; 315:1455-1458

7. Holst E, Wathne B, Hovelius B, et al: Bacterial vaginosis: Microbiological and clinical findings. Eur J Clin Microbiol 1987; 6:536-541

8. Spiegal CA, Amsel R, Eschenbach D, et al: Anaerobic bacteria in nonspecific vaginitis. N Engl J Med 1980; 303:601-607

9. Spiegal CA, Eschenbach D, Amsel R, et al: Curved anaerobic bacteria in bacterial (nonspecific) vaginosis and their response to antimicrobial therapy. J Infect Dis 1983; 148:817-822

10. Leighton PM: *Gardnerella vaginalis:* Laboratory identification and clinical significance. J Public Health 1982; 73:335-340

11. McCormack WM, Hayes CH, Rosner B, et al: Vaginal colonization with *Corynebacterium vaginale (Haemophilus vaginalis).* J Infect Dis 1977; 136: 740-745

An Effective Clinical Approach to Vaginismus—Putting the Patient in Charge

VAGINISMUS is an involuntary spasm of the introital muscles in anticipation of vaginal penetration. Classically, its severest form makes penetration virtually impossible and causes a severe, burning pain. But there are less pronounced degrees of vaginismus, characterized by a "stiffening" of the vaginal musculature, allowing penetration, yet accompanied by the same sort of pain. The condition may be primary (present from the first attempt at penetration) or secondary (following physical or psychological trauma, infection, menopausal changes, or pelvic pathology).

Although the incidences of primary and severe vaginismus (prohibiting penetration) are relatively low, secondary vaginismus and introital "guarding" are seen reasonably frequently in clinical practice. Modern treatment methods approach 100% success, given the outcome criteria described by Kaplan. The technique detailed herein is a useful refinement.

The diagnosis of vaginismus can only be verified by physical examination and after other causes of local pain or atrophy have been treated or ruled out. These include the obvious and subtle causes of superficial dyspareunia, such as anatomic abnormalities, infections, mucosal tears, hypersensitive scars, atrophic vaginitis, inadequate lubrication, painful hymeneal tags, urethral caruncle, topical allergies, focal vulvitis, postherpetic neuralgia, and hypersensitivity to a partner's semen.

On physical examination, the patient is tense, the buttocks tight, the thighs adducted, and the perineum taut and contracted. The treatment is based on several prerequisites:

- The cause of the condition—determined by history—must be explained to the patient, as must its mechanics.
- The patient must be motivated to enjoy coitus or desire to effect painless vaginal insertion for other reasons—self-acceptance, the use of tampons, comfort during medical examinations.
- The patient must learn that she can be in control of her vagina at all times during treatment.
- The patient—and her partner—must be willing to patiently undergo a progressive process of systematic desensitization and counseling.

Treatment begins with the pelvic examination. The patient is assured that she is in control: When she says, "Stop," the examiner always stops. It may take several sessions to demonstrate painless vaginal insertion. The wait is worth it in the long run. The patient is taught the Kegel exercises, with special attention to bearing down and pulling in. When she can do this easily, the examiner (with the patient's permission) gently places the tip of the index finger at the introitus, asking the patient to bear down or "push the finger away." Repeating this exercise several to many times, with rest periods, should eventually result in the fingertip being "captured" by the vagina (as opposed to the vagina being "penetrated")—an active, rather than passive process. The patient comes to realize that she can be in active control of what enters her vagina and is usually astonished to discover that it is painless. Patience, gentleness, and time will permit the length of a finger to be "captured" in this way. The same procedure is repeated by the patient herself and, if possible, by her partner. Graduated vaginal dilators are substituted for the finger at home and are left in place for 15 to 60 minutes at